Summary

In a patient who probably had had rheumatic heart disease, bacterial endocarditis caused by *H. aphrophilus* developed years later. The infection was successfully treated with parenteral ampicillin and streptomycin. Bacteriological data, and in vitro antibiotic sensitivity studies are presented. The eight previously reported cases of bacterial endocarditis caused by this organism are reviewed with treatments compared, including one case treated with ampicillin. The role of this organism in other human infections with the proportion of positive cultures from various sources as confirmed by the Communicable Disease Center, Atlanta, Georgia, is presented. Available data suggest ampicillin is effective in treating infections caused by this organism.

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GENERIC AND TRADE NAMES FOR DRUGS

Ampicillin—*Polycillin-N.*
Cephalothin—*Keflin.*

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Hodgkin's Disease Terminating in Chronic Myeloid Leukemia

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HODGKIN'S DISEASE is an ever popular subject in the medical literature because of its protean manifestations and the diversity of its course. It was first described in 1832 by Thomas Hodgkin as "a disorder affecting the absorbent glands and spleen," and its cause has yet to be determined.[18] Although it is classed with the malignant lymphomas the histologic character of Hodgkin's disease bears

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strong resemblance to an infectious granuloma rather than to a neoplasm.[2] Unlike the other lymphomas it rarely terminates in leukemia. A review of the literature indicates an occasional case report of Hodgkin's disease occurring simultaneously with Kaposi's sarcoma,[4,9] multiple myeloma[8] and with other malignant disorders.[14] Only two cases of myeloid leukemia have been reported coexistent with Hodgkin's disease.[15] The following case report is of interest because of the relatively long survival of a patient with Hodgkin's disease who later had chronic myeloid leukemia. Whether radiation was a factor in the development of the leukemia will be discussed.

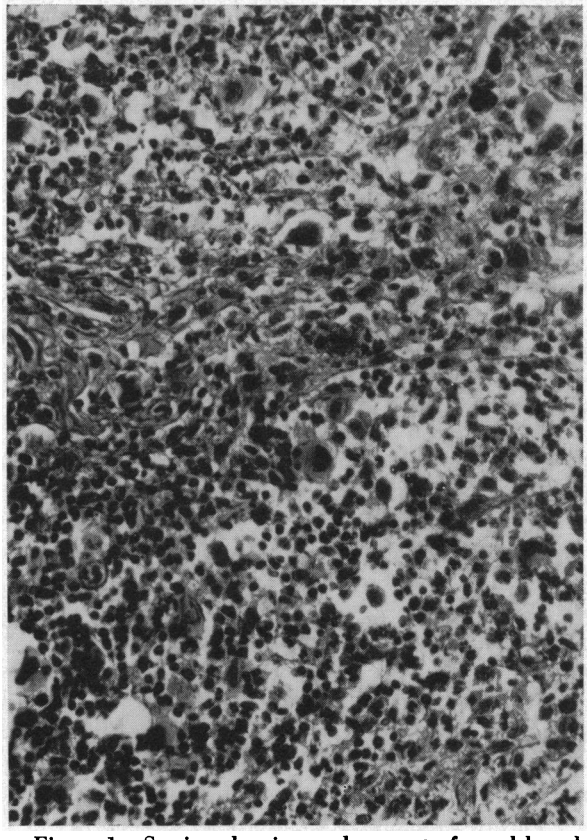

Figure 1.—Section showing replacement of usual lymph node architecture by reticulum cells with a mixture of lymphocytes, eosinophils, polymorphonuclear cells, plasma cells and a profusion of Reed-Sternberg cells (Hematoxylin eosin stain, ×250).

Report of a Case

A 39-year-old Caucasian housewife noted a left axillary mass in September 1953. Because of fatigability, a 10-pound loss in weight and development of a mass 0.5 cm in diameter in the left clavicular area, she was referred to the University of California Medical Center in February 1954. The mass was removed and microscopic examination showed replacement of the usual lymph node architecture by reticulum cells and a profusion of Reed-Sternberg cells typical of Hodgkin's granuloma (Figure 1). An x-ray film of the chest showed a small left pleural effusion and a large lobulated anterior mediastinal mass (Figure 2). An abdominal scout film showed obliteration of the right psoas shadow, hepatomegaly and an enlarged spleen. Leukocytes numbered 12,750 per cu mm and hemoglobin concentration was 70 per cent. Radiation therapy was begun 2 March 1954. A detailed account of the courses of radiation is given in Table 1. A tumor dose of 1,000 r was given to the mediastinum and a tissue dose of 1,500 r to the left axilla. Follow-up appointments in the outpatient clinics showed progressive decrease in adenopathy (Figure 3) and on 9 December 1964, physical examination was within normal limits. In June 1955, a 4 × 4 cm left supraclavicular node was noted; 1,000 r was given and the node promptly disappeared. In August 1956, right cervical adenopathy appeared and it also responded to radiation therapy. The patient

TABLE 1.—*Details of X-Radiation*

Date	*Number of Treatments*	*Location*	*Field*	*r in Air*	*r to Skin*	*r to Tissue Calculated at 3 cm in Depth*
3/2/54-3/23/54	16 (22 days)	Anterior mediastinum	10×15 cm	1,700	2,500	1,000 (tumor)
		Posterior mediastinum	10×15 cm	700	900	
3/16/54-3/25/54	8 (10 days)	Left axilla	10×10 cm	1,500	1,900	1,500 (tissue)
6/13/55-6/18/55	6	Left supraclavicular	7×7 cm	1,100	1,350	1,000 (tissue)
8/2/56-8/ 7/56	5	Right cervical	7×7 cm	1,100	1,350	1,000 (tissue)
10/7/60-12/3/60	31 (44 days)	Right supraclavicular	9×13 cm	5,048	5,550	4,455 (midplane)
	32 (47 days)	Right axilla	9×9 cm	4,982	5,450	
	40 (59 days)	Anterior mediastinum	20×9 cm	5,088	5,700	
		Posterior mediastinum	20×9 cm	3,392	3,800	

Technical factors: 250 KVP, 30 MA, 1.4 mm. CU HVL, 50 cm. TSD, 0.5 mm. CU + 1.0 mm. AL filter. Tumor dose equals dose at the midplane. Tissue dose calculated at 3 cm in depth.

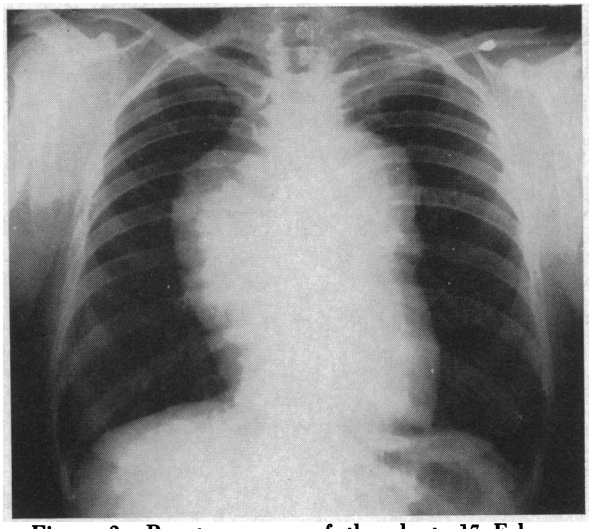

Figure 2.—Roentgenogram of the chest, 17 February 1954, showing a large lobulated anterior-superior and anterior-middle mediastinal mass.

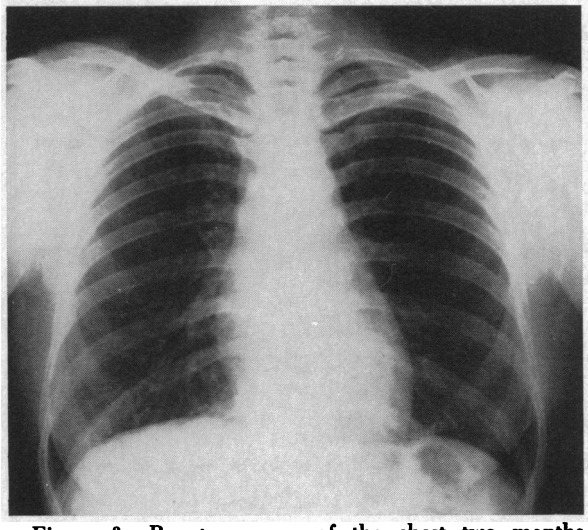

Figure 3.—Roentgenogram of the chest two months after completion of initial course of radiation therapy, showing complete regression of the mediastinal mass.

was seen every two months and remained asymptomatic with no abnormality noted on physical examination, blood studies or roentgenograms of the chest until 30 June 1960, when an x-ray film showed mediastinal widening, and a right axillary node was palpable. Radiation therapy was given to the right axilla and to the mediastinum during the fall of 1960.

The patient felt well, and physical examination and hemogram were normal until June 1961, when leukocytes numbered 18,500 per cu mm. She was seen at monthly intervals thereafter until October 1961, when she was admitted to the Cancer Research Institute of the University of California Hospitals because of progressive increase in the leukocyte count. Hematologic changes are listed in Table 2.

On admission to the hospital she appeared well developed and well nourished and was without symptoms. There was radiation erythema over the chest, back, arms and neck. A 0.5 × 1 cm left supraclavicular node was palpable. There was no sternal tenderness. The spleen was palpable 3 cm below the left costal margin. The remainder of the physical examination was normal. Laboratory studies showed leukocytes numbering 132,600 per cu mm, the hematocrit at 35 per cent, and platelets numbering 835,000 per cu mm with many large bizarre forms. Urinalysis was within normal limits. Results of a bromsulphalein test and of determinations of blood chemical factors, including calcium, phosphorus, glucose, creatinine and serum protein, were within normal limits. The uric acid content was 8.1 mg per 100 ml. The leukocyte alkaline phosphatase was 2 per cent positive. Papanicolaou studies of cervical smears were negative for neoplasm. An intravenous pyelogram showed a normal urinary collecting system; enlargement of the liver and spleen was noted. An x-ray film of the chest showed slight prominence of the right superior mediastinum. A bone survey was negative for metastatic disease. Marrow aspirated from the iliac crest showed increase in the myeloid series with an increase in promyelocytes. A diagnosis of chronic granulocytic leukemia was established and on 8 November 1961 treatment with busulfan (Myleran®), 2 mg twice a day, was begun.

The patient was observed at regular intervals in the Cancer Research Outpatient Clinic and she responded well to busulfan therapy. Except for herpes zoster developing at the level of the twelfth thoracic vertebra in December 1962, the patient felt well and had no other complications until October 1963, when it was noted that the hematocrit was gradually decreasing. On 13 November 1963 she was admitted to the Cancer Research Institute because of fatigue, frequent colds and edema at the ankles. She was alert and pale but apparently in no distress. There was no enlargement of nodes. The liver was palpable 7 cm below the right costal margin and the spleen 3 cm below the left costal margin. There was 3 plus pedal edema.

The hematocrit was 20.5 per cent. Leukocytes numbered 12,150 (54 per cent polymorphonuclear, 16 per cent band cells, 5 per cent meta-

TABLE 2.—*Hematologic Data for Last Three Years of Patient's life*

Date	*Leukocytes (per cu mm)*	*Hgb (gm per 100 ml)*	*Hematocrit (Vol per cent)*	*Lymph Per Cent*	*PMN's Per Cent*	*Nonseg Per Cent*	*Eos Per Cent*	*Baso Per Cent*	*Mono Per Cent*	*Meta Per Cent*	*Myelo Per Cent*	*Promyel Per Cent*	*Platelet per cu mm³*
10/10/60	7,900	12.8	42	12	76	....	1	....	11	....	....	....	adequate
11/13/60	5,400	12.8	40	3	81	1	3	....	12	....	....	....	adequate
12/15/60	6,500	11.6	35	....	....	....	....	....	....	....	....	....	.....
3/16/61	7,500	11.6	.....	....	....	....	....	....	....	....	....	....	.....
6/15/61	18,500	11.9	.....	....	....	....	....	....	....	....	....	....	.....
6/28/61	22,850	11.4	.....	32	63	1	1	2	1	....	....	....	.....
7/27/61	31,500	12.9	41	16	63	7	5	4	5	....	....	....	adequate
8/10/61	45,500	12.3	41	5	66	10	1	3	3	8	4	....	.....
9/26/61	92,000	11.4	41	....	....	....	....	....	....	....	....	....	.....
10/31/61	132,600	11.5	35	1	38	25	2	3	3	22	5	1	835,000
11/ 8/61	148,500	11.3	34	1	33	14	1	5	1	36	7	2	1,245,000
11/16/61	152,000	10.2	34	....	34	23	4	4	1	16	11	7	1,075,000
11/30/61	64,175	10.9	.....	2	52	11	2	4	....	6	5	18	745,000
12/14/61	25,500	10.8	36.7	1	72	6	4	8	5	....	....	4	815,100
12/28/61	13,700	11.2	36.1	1	75	6	3	2	4	6	2	1	467,000
4/19/62	8,450	13.5	43.5	6	83	3	3	4	1	....	....	....	415,000
7/12/62	31,650	13.8	46	....	71	3	4	1	1	10	10	....	665,000
9/ 6/62	34,250	14	41.5	2	56	17	2	3	1	10	2	7	2,295,000
10/18/62	16,050	12.5	37.6	5	76	3	2	4	3	3	4	....	869,000
12/27/62	18,450	13.3	41.2	4	71	5	4	5	8	1	2	....	1,000,000
2/ 7/63	7,900	11.5	37.2	....	....	....	....	....	....	....	....	....	.....
2/21/63	6,850	11.6	35.2	....	....	....	....	....	....	....	....	....	.....
3/ 7/63	10,000	11.8	37.8	....	....	....	....	....	....	....	....	....	.....
6/ 4/63	20,550	11.9	37.8	2	82	4	1	2	2	5	1	1	1,376,000
8/27/63	11,600	12.2	40	3	73	3	1	6	6	2	4	2	424,000
9/10/63	9,600	11.8	37.5	3	57	3	5	11	14	5	1	1	455,000
10/ 8/63	28,100	10.6	35.2	1	41	6	3	10	4	9	13	13	620,000
10/22/63	27,550	8.7	28	6	43	1	7	3	4	6	20	10	315,000
11/12/63	15,200	6.9	20	8	36	8	3	4	....	6	25	10	300,000
12/ 5/63	30,350	7.8	24.5	1	24	5	3	4	1	25	30	7	650,000
12/12/63	14,850	6.0	18.4	2	30	10	6	....	2	11	22	7	334,000
12/26/63	3,100	....	.....	4	64	3	2	1	....	15	10	1	.....

myelocytes, 7 per cent myelocytes, 10 per cent promyelocytes, 3 per cent eosinophils, 1 per cent basophils, 3 per cent lymphocytes, 1 per cent monocytes) and platelets 499,000 per cu mm. The urine showed a trace of protein and there were 15 to 20 leukocytes per high power field. The serum protein was 5.4 gm per 100 ml with an electrophoretic pattern showing a decrease in the albumin component (53.2 per cent). The bilirubin was 0.2 mg, calcium 8.8 mg, phosphorus 4 mg, uric acid 5.6 mg, and blood urea nitrogen 11.4 mg per 100 ml. Bromsulphalein retention was 10 per cent in 45 minutes. The serum iron was 81 mcg per 100 ml, with total iron-binding capacity of 254 mcg per 100 mg. The result of a Coombs' test (direct and indirect) was negative. The urobilinogen content of the stool was 111 mg in 72 hours. An erythrocyte survival determination with Cr^{51} showed a half-time of 17.5 days (normal 25 to 40 days). Erythrocyte cholinesterase was 1.17 units (normal 0.80 to 1.20). Marrow aspirated from the iliac crest showed generalized hypoplasia with a decrease in the erythrocytic precursors and megakaryocytes. The predominant cell type was a myelocyte. There was no significant shift to the left. A roentgenogram of the chest showed a slightly widened right paratracheal shadow and an increase in the size of the heart.

It was the consensus that the patient had chronic granulocytic leukemia with diminished red blood cell production and that a hemolytic component also was playing an etiologic role in the anemia. A transfusion of two units of whole blood was given and treatment with 6-mercaptopurine, in dosage of 50 mg a day, was begun just before the patient was discharged from the hospital 30 November 1963. When she returned to the clinic on 12 December 1963, the hematocrit was 18.4 per cent. Prednisone, 60 mg per day, was started. Two weeks later the hematocrit was still low and the leukocyte count had dropped to 3,100 per cu mm with no significant increase in immature forms. Prednisone was continued but the use of 6-mercaptopurine was stopped.

The patient died at home on 1 January 1964. Permission for autopsy was not granted.

Discussion

It has been recognized that the malignant lymphomas (lymphosarcoma, reticulum cell sarcoma, giant follicular lymphoblastoma and Hodgkin's disease) and lymphatic leukemia are closely related. Sternberg, in 1908, recognized "leukemic blood" in cases of lymphosarcoma, and transition forms from one to another have been encountered.[1] The incidence of leukemic transition in a series of 1,269 patients with lymphosarcoma has been reported as 7.6 per cent.[16] There are few reports of leukemia, other than lymphatic leukemia, occurring spontaneously in lymphoma; the reported cases have usually followed radiation therapy.[3,11,19]

That radiation exposure in man is associated with an increased incidence of leukemia has been well documented.[6,10,13] Analysis of persons exposed to atomic radiation[12] and patients irradiated for ankylosing spondylitis[7] indicates that acute leukemia and chronic myeloid leukemia may be caused by radiation under certain conditions. There is some evidence that fractionated and repeated irradiation may be more leukemogenic than that given in a single episode.[17,20] When leukemia is related to radiation, at least 12 to 18 months elapse between irradiation and onset of leukemia.[5]

In the case here reported, radiation therapy was begun in March 1954 and intermittent courses were given until December 1960. The peripheral blood remained normal until June 1961. It is believed that the terminal illness was due to cumulative effects of radiation therapy rather than to a spontaneous occurrence. The development of myeloid leukemia in patients with Hodgkin's disease who have not received irradiation is so rare that it can be considered fortuitous. Both the literature and the present case suggest that myeloid leukemia in patients with Hodgkin's disease is related to therapeutic exposure to x-rays.

Although radiation is curative in localized Hodgkin's disease and is certainly the treatment of choice initially, discretion should be used in the total amount administered.

Summary

A case in which a patient with Hodgkin's disease was treated with high dose radiation therapy is reported. After seven and a half years of satisfactory control, chronic myeloid leukemia developed. The patient at first responded well to Myleran® therapy but after 23 months refractory hemolytic anemia developed and the patient died.

It is postulated that the development of chronic myeloid leukemia was a consequence of the radiation therapy.

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GENERIC AND TRADE NAMES OF DRUGS

Busulfan—*Myeleran.*

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Tuberculous Tenosynovitis In a Patient with Hyperuricemia

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TUBERCULOUS TENOSYNOVITIS is uncommon. Even when tuberculosis was highly prevalent, Adams and coworkers[1] found that during a 45-year period only 36 patients were admitted to the Massachusetts General Hospital with this disease (one case per 7,891 admissions). Although the incidence of tuberculosis has decreased dramatically since the advent of anti-tuberculosis drugs, tuberculous tenosynovitis still occasionally occurs and may mimic the more frequently seen metabolic or rheumatic diseases.

Report of a Case

A 53-year-old white woman was first seen at the University of California Surgical Clinic in April 1964 because of recurrent swellings and masses on the left hand and wrist. The swelling had been present since December 1961, and was associated with throbbing pain, loss of sensation in the fingertips and weakening of grasp. The patient had been treated with cortisone by another physician but with only slight improvement.

In July 1962 painless masses appeared on the dorsal and volar aspects of the wrist, hand and dorsal forearm. Biopsy showed widespread granulomata, Langhans' giant cells and epitheloid cells compatible with tuberculosis or sarcoid. She had no history of pulmonary tuberculosis but she had drunk raw milk when she was a child and had a 30-year history of pain, crepitus and limitation of motion of the left hip. She had had stage II carcinoma of the cervix 10 years previously, which was treated by radium. She was treated with strep-

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